Surgical Aspects of Intestinal Injury Due to Pelvic Radiotherapy

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Seventy-one patients with intestinal injury secondary to pelvic irradiation had predominantly large bowel lesions. Seventeen cases were treated conservatively and 54 came to surgery, 28 patients having more than one operation. Following this essentially salvage surgery there were more ileal than colonic anastomotic leaks. Thirty-four patients died during the follow-up period (2–12 years), 19 from recurrent malignancy, and nine as a result of continuing radiation effects. Seventy per cent of the patients who had a radiation fistula died as a result of malignancy. Of 4200 cases of pelvic malignancy treated by irradiation over the decade 1972–1982, surgical referrals for complications constituted 1.7%, with an overall radiation-related mortality of 0.2%. It is our opinion that colostomy alone has little part to play in this condition, and a policy based on excisional surgery is suggested.

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RADIOTHERAPY PLAYS an important part in the treatment of many abdominal and pelvic malignancies, including carcinoma of the cervix, bladder, and more recently, rectum.[1] The radiation dose that can safely be administered is limited by the tolerance of the surrounding pelvic and abdominal tissues. Fifty per cent to 70% of patients suffer from acute side-effects,[2] the majority of which respond to medical measures. Chronic radiation damage may affect sigmoid colon, rectum, cecum, ileum, and bladder, and two per cent to 17% of patients may require surgery for late complications at these sites.[3–5] The incidence of radiation damage is rising with modern techniques, as increasing field sizes are employed in an attempt to improve cure rates.[6,7] This study examines the pattern of radiation injury of the intestine, its management, and its outcome in patients treated in one surgical unit. Anseline et al.[8] have suggested a conservative approach to fistulae, strictures, and proctitis by proximal colostomy. Our evidence is that a more radical approach is beneficial.

Patient Group

Between July 1972 and December 1982, 71 patients were referred to the Department of Surgery at the Western General Hospital, Edinburgh, with intestinal complications attributable to pelvic irradiation. These cases have been reviewed, and the diagnosis of radiation-induced injury accepted only if histological evidence was available on biopsy (Fig. 1) or surgically resected specimen (Fig. 2), or if typical radiological appearances were seen (Fig. 3).

The group comprised 16 male and 55 female patients aged 36 to 82 years. The primary sites of tumour for which the patients had received radiation therapy are shown in Table 1, almost half having been treated for cervical carcinoma. Most patients received 3000–5500 centigrays as external beam radiotherapy, and for patients with carcinoma of the cervix this was followed by intracavitary insertions of radium or cesium. Two patients with carcinoma *in situ* of the cervix had intracavitary therapy alone.

Results

The majority of patients presented to the surgical unit with abdominal pain and altered bowel habit (Table 2), with associated blood or mucus in the stools of those with damaged sigmoid colon or rectum. Late nausea and vomiting were mostly associated with small bowel injury. Chronic gastrointestinal symptoms were evident a median of 4.2 months postradiotherapy, and a median of 5.9 further months elapsed before surgery. Figure 4 shows that the rectum and sigmoid colon were most often the site of radiation damage, followed by the ileum and cecum. The nature of the pathology is shown in Tables 3 and 4. Stricture was the most common complication in the sigmoid colon, and fistulae were commonly located in the ileum or rectum.

Conservative Group

Fifteen patients were successfully managed conservatively with medical measures, including parenteral nutrition, steroids systemically or by enema, transfusion

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for blood loss, and intravenous fluids and nasogastric suction for episodes of obstruction. Bulking agents and dietary agents were occasionally of some benefit. A further patient had diathermy of a radiation ulcer in the rectum, and one other had the rectum packed for hemorrhage from a similar lesion.

Surgical Group

Fifty-four patients did not respond to conservative measures and required surgery: 18 patients had two operations, four had three operations, four had four operations, and two patients had five operations. Two additional patients had diagnostic laparotomy only and are not included in the analysis. Forty-three patients (80% of operated cases) had one or more bowel resections: 25 of these had a colostomy prior to, or at the time of resection, and this was subsequently closed in 15 patients. Colostomy without resection was performed in eight cases, and all of these patients were left with a permanent stoma. Twenty-four patients had one or more colocolic or colorectal anastomoses; these included eight cases who had the whole rectum excised with sphincter preservation by a sleeved coloanal anastomosis.[9] Ten patients had ileocolic anastomoses and nine ileoileal anastomoses. Eleven patients developed 23 fistulae, 20 involving the gastrointestinal tract (Table 4).

Anastomotic Problems

Four cases of established anastomotic leakage occurred in 48 anastomoses—three out of ten ileocolic anasto-

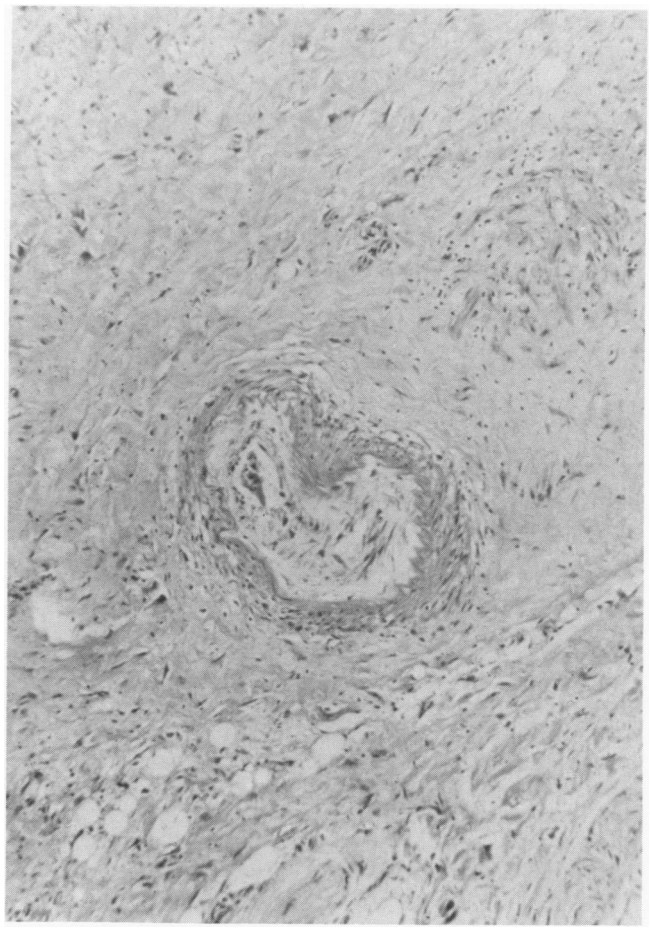

FIG. 1. Biopsy of colonic wall. Subserosal vessel with chronic endarteritis and intimal fibrosis. Atypical fibroblasts with dense nuclei can be seen in the periphery.

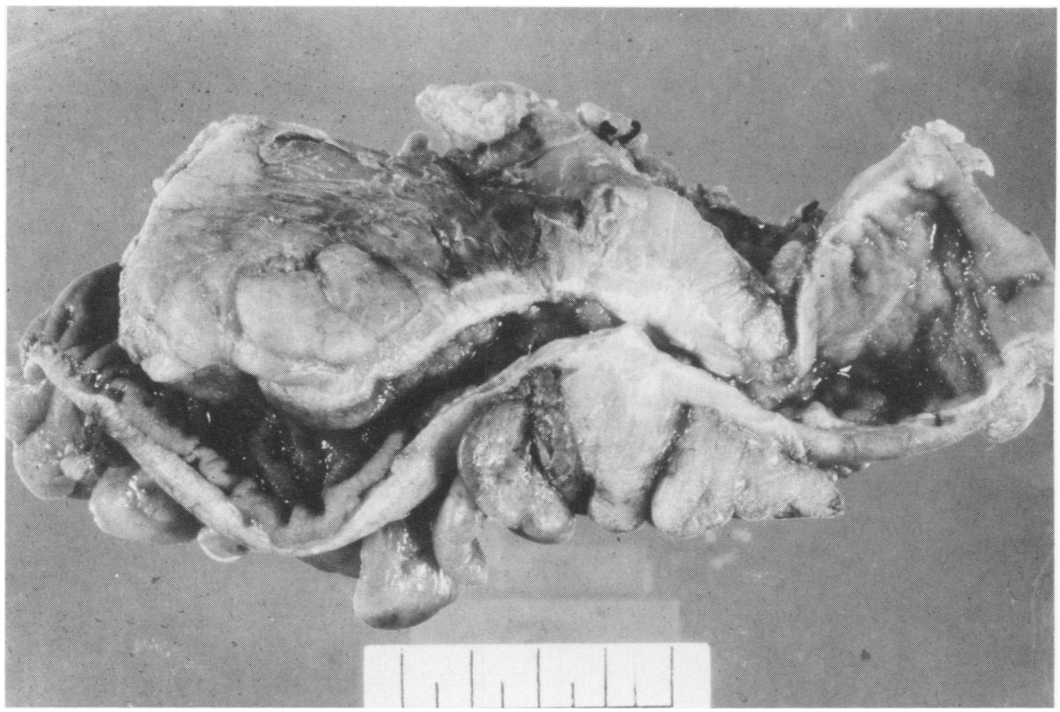

FIG. 2. Resected radiation stricture. Surgical specimen with edema and fibrosis extending beyond the stricture towards the surgical margins.

FIG. 3. Barium enema. 6500 centigrays to cervical carcinoma resulted in stricture, with radiation damage extending proximal to the stricture, resulting in shrinkage and loss of the pelvic colonic loop.

moses leaked and all three patients died. One of the nine ileoileal anastomoses leaked and further resection was followed by a small bowel fistula that closed with conservative management. Although no colocolic, colorectal, or coloanal anastomotic leak was proven, three patients developed postoperative pericolic abscesses, and these may well represent cases of minor leakage. One patient whose ileal stricture was bypassed by ileotransverse anastomosis developed a fistula to the bladder and died of septicemia. No patient required revisional surgery for stoma problems.

TABLE 1. *Diagnosis for Which Radiotherapy Was Given*

Diagnosis	No. Patients
Carcinoma cervix	35
Carcinoma bladder	19
Colorectal carcinoma	7
Carcinoma prostate	3
Carcinoma ovary	3
Carcinoma uterus	1
Carcinoma anus	1
Hodgkin's disease	1
Postmenopausal bleeding	1
Total	71

TABLE 2. *Presenting Symptoms of Side-Effects of Pelvic Irradiation*

Symptoms	No. Patients
Abdominal pain	57
Diarrhea	51 (6 with fecal incontinence)
Constipation	50
Bleeding per rectum	41
Tenesmus/mucus per rectum	25
Nausea/vomiting/anorexia	33
Urinary symptoms	24

Unsuccessful Surgery

In a total of nine further patients, surgery was considered to have been unsuccessful, and these are detailed as follows. Three patients who had anterior resections developed recurrent stricture; one of these patients underwent further resection and one had a permanent loop sigmoid colostomy. Three further patients who had a resection developed recurrent proctitis requiring permanent defunctioning colostomies. One patient had a temporary colostomy closed which had to be reestablished due to recurrent rectal stenosis. A case of rectovesical fistula treated by Hartmann's procedure later required abdominoperineal excision of the rectum on account of a fistula from the rectal stump to the cecum, and subsequently died of pelvic sepsis and hemorrhage. A further patient with a rectovesical fistula who initially had a transverse colostomy died from massive hemorrhage per rectum.

Deaths

Thirty-four patients had died by the end of the study in December 1983. Of the remainder, 31 had been followed for more than 2 years following completion of

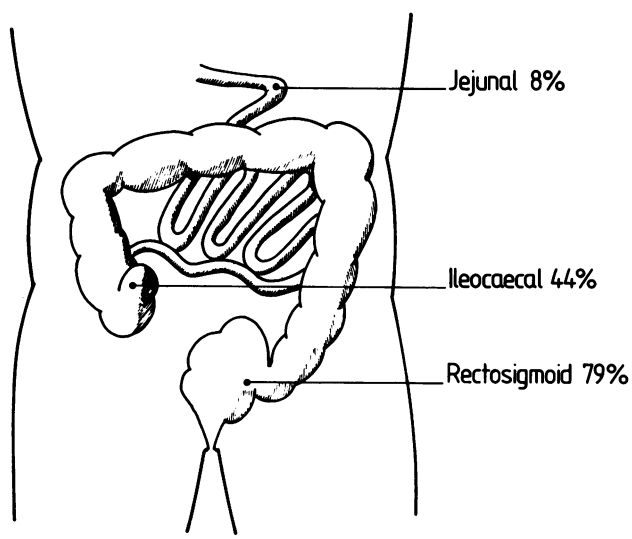

FIG. 4. Sites of radiation damage (71 patients).

radiotherapy, 17 for more than 5 years, and 12 for more than 10 years. Of those who succumbed, six died from incidental causes, 19 from recurrent malignancy, and nine from side-effects of irradiation.

Three of the nine whose death was attributable to the complications of radiotherapy died as the result of ureteric obstruction: two of these had septicemia (one of whom also had an ileovesical fistula), and one had renal failure. Three further patients died from massive hemorrhage associated with uncontrolled pelvic sepsis, and three had an anastomotic dehiscence with peritonitis.

Discussion

During the decade 1972–1982, approximately 4200 patients received pelvic irradiation in the Department of Radiation Oncology of the Western General Hospital in Edinburgh, and 71 of these patients (1.7%) were referred to the Department of Surgery. In recent years in the management of pelvic malignancy there has been a tendency to increase the treatment field size with the aim of improving cure rates. The incidence of intestinal complications has increased,[6,7] in spite of more accurate estimation of dosage and the introduction of central pelvic shielding. Most patients (74% in our hospital) suffer acute side-effects such as diarrhea or vomiting during and immediately after treatment, but in the majority these settle with symptomatic measures. While some patients have continuing bowel symptoms, most have a respite for some months before serious radiation damage becomes apparent. In this study some patients were asymptomatic for as long as 4½ years. The mean time of referral for surgical opinion was 28 months (median 4.2 months) after irradiation. Jackson[10] also found that the majority of patients had symptoms within 1 year of radiotherapy, whereas Kwitko et al.[11] found a mean interval of 4.7 years.

The patients reported here represent a selected group with symptoms severe enough to warrant surgical referral, with 76% coming to major surgery. A quarter of patients considered for surgery, however, improved sufficiently on medical measures for this to be avoided. It has been estimated that 2.6% of patients may require surgery for complications following pelvic irradiation,[6,7] but only 54 (1.3%) of the 4200 patients irradiated in this study came to operation. The delay in the onset of symptoms and the further interval prior to surgery mean that many patients wait around a year after radiotherapy before surgical intervention. This allows time for differentiation between those with progressive malignancy and those whose main problem is radiation damage.

Many patients had both large and small bowel injury, but rectal and sigmoid problems predominated, perhaps because the rectum and lower sigmoid are fairly immobile and therefore receive more continuous irradiation. The type of lesion varied according to the area affected: stricture was seen more commonly in colorectal damage and fistula in the ileum. Almost half of the patients who required surgery had had previous intraperitoneal surgery, and it has been suggested that adhesions may immobilise loops of bowel in the pelvis, making them especially susceptible to radiation damage.[12] Moss et al.[13] found

TABLE 3. *Nature of Radiation-Induced Pathology and Surgical Management*

Radiation Damage to Sigmoid Colon and/or Rectum (56 Patients)
Inflammation only (18)
8 Resections (4 permanent and 2 temporary colostomies)
2 Colostomy only (permanent)
8 Managed conservatively
Stricture (32)
18 Resections (4 permanent and 9 temporary colostomies)
4 Colostomy only
10 Managed conservatively
Radionecrosis and perforation (3)
2 Resections (1 permanent and 1 temporary colostomy)
1 Permanent loop colostomy
Fistulae (5)
(See Table 4)
Radiation Damage to Ileum/Cecum (32 Patients)
Inflammation only (9)
3 Resections
6 Managed conservatively
Obstruction Due to Adhesions or Stricture (10)
5 Resections (one subsequent ileotransverse bypass)
2 Bypass (ileotransverse anastomosis)
3 Division adhesions
Radionecrosis and Perforation (6)
All resected
Fistulae (10)
(See Table 4)

TABLE 4. *Fistulae Following Pelvic Radiation (11 Patients)*

Ileocolic (4)
3 Excised
1 Closed spontaneously
Recto-/Colo-vesical (4)
All had colostomy carried out, which was not closed.
Ileocutaneous (3)
2 Resections
1 Managed conservatively (recurrent carcinoma)
Colocutaneous (2)
1 Resection
1 Managed conservatively (recurrent carcinoma)
Vesicovaginal (2)
1 Ileal conduit
1 Managed conservatively (recurrent carcinoma)
Ileovesical (2)
Both managed conservatively
Cecorectal (1)
Abdominoperineal excision of rectum
Colovaginal (2)
Colostomy
Ileovaginal (1)
Resection
Vesicocutaneous (3)
Ileal conduit

that 25% of patients with gastrointestinal complications of radiotherapy for carcinoma of the cervix had had previous surgery. Kwitko et al.[11] found that 24 out of 31 patients with ileal damage had previously had pelvic surgery, but in this study, at ten out of 21 patients, the proportion with previous surgery who developed small bowel damage was the same as the proportion who had rectosigmoid damage.

Eleven patients with rectosigmoid injury had a loop sigmoid colostomy alone as the initial treatment. In three cases this was done because disseminated malignancy was found at operation, and none survived more than 6 months. Of the remaining eight, two declined further surgery, but two died of pelvic sepsis and hemorrhage, and four required further surgery for persistent symptoms. It therefore appears that a proximal colostomy does not prevent progression of radiation changes in the defunctioned bowel, and indeed closure of such a colostomy is often followed by recrudescence of symptoms,[14] as happened in three patients in this series. No patient in this study required surgery for complications of a colostomy itself, and this contrasts with the experience of Deveney et al.,[15] who reported that seven out of 32 patients with a colostomy developed necrosis and paracolostomy fistulation. It is clearly important to choose healthy bowel for formation of a colostomy.

Like defunctioning colostomy, bypass of a diseased segment of bowel may allow progression of radiation damage. It was the policy in this series to excise affected bowel whenever possible. Three patients, however, did have ileotransverse anastomoses to bypass ileocecal disease: two did well, but one patient developed a fistula from the bypassed ileum into the bladder and died from septicemia. Poor results from bypass have been reported by others,[7,14] who recommend that it should be avoided, but Lillemoe et al.[16] reported good results in nine out of 11 patients who had damaged ileum bypassed.

While left-sided colonic anastomoses are considered less secure than those in other sites in nonirradiated patients, all four cases of established anastomotic dehiscence in this series occurred among the 19 ileal anastomoses (ileocolic or ileoileal). In contrast there was only suspected leakage in three of 28 colonic anastomoses (colocolic, colorectal, or coloanal). When grossly diseased distal ileum is excised, the integrity of the anastomosis may be prejudiced by a minor degree of radiation damage more proximally, not apparent to the naked eye. The greater mobility of the small bowel increases the likelihood of fairly proximal small bowel coming down into the pelvis and hence being exposed to radiation effects. Colocolic and colorectal anastomoses were less subject to such problems because the colon brought down for an intrapelvic anastomosis is commonly the transverse colon and, as such, well away from the radiation area. Eight coloanal anastomoses were performed to eradicate distally placed disease, and all healed well without undue problems, although later one had to have an anastomotic dilatation.

It is clearly important to examine carefully the nine deaths resulting from the side-effects of radiation. The three patients with anastomotic leakage have already been discussed. Of those remaining, in three cases fibrosis and inflammation in the pelvis resulted in ureteric obstruction, and urinary sepsis or failure. In one of these patients, repeated attempts to fashion an ileal urinary conduit had been unsuccessful due to extensive small bowel damage. Uncontrolled sepsis always carries the risk of erosion of major vessels, and three patients died from hemorrhage in the presence of pelvic sepsis. Two of these had rectovesical fistulae which had been managed by defunctioning colostomy alone, and the third had a pelvic abscess following four operations for multiple fistulae. Only one of the nine patients who died directly from the effects of radiation had overt recurrent malignancy at the time of death.

The 11 patients with fistulae form a more complex group. Eight of these died of recurrent malignancy by the end of the study, indicating that they constitute a group with a poor prognosis regardless of the radiation problems, and suggesting that the presence of a fistula implies wider dissemination of the malignant process than may be recognized at first.

A reduction in the incidence of complications of pelvic irradiation might be achieved by decreasing the radiation dose. This, in the view of most radiation oncologists, would inevitably lead to a higher incidence of recurrent malignancy. To avoid this in turn, and maintain a thorough standard of tumor treatment, it seems that an incidence of complications from radiotherapy must be accepted.

Most of the effects of radiation in the gastrointestinal tract settle spontaneously, and it must be emphasized that serious complications affect only a small proportion of patients whose cancer has been effectively treated by radiotherapy. The majority of problems arising in patients referred to surgical units are, however, grievous enough to require remedial surgery. By delaying intervention in many instances, it becomes clear whether the principal problem is one of recurrent malignancy or radiation damage. This work suggests that, contrary to the findings of Anseline et al.,[8] direct surgical excision can eliminate diseased bowel with comparative safety. The number requiring such surgery is relatively small—over 98% of patients treated for pelvic cancer by irradiation never develop chronic problems. The results of excision of irradiated left colon in our series lead us to believe that the risks of anastomotic dehiscence are less than those for small bowel anastomosis following irra-

diation, which is a reversal of the accepted pattern. The most difficult area is surgery for fistulae. Although this may at first appear successful, over two-thirds of patients may be expected to succumb to recurrent malignancy. Yet the relief of symptoms by palliative surgery makes operation worthwhile in this group also.

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